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EDITORIAL

REGULATED, RESPONSIBLE COSMETICS

SOME years ago we penned a lengthy though perhaps lean lecture on the—"Cosmetic Urge." Since then the urge has evolved from urge to splurge, to scourge—and the lecture then thought adequate is now a scant and sheer history.

Never in all the world has the business of "inciting to beauty" found so wide an application.

Ever since Eve revealed her wanton weakness and ate her Adam out of house and home—women, the world over, have tried to improve on nature—and with more or less success. Chart the course of history and learn how beauty ruled when even reason failed. Recall the Roman days—and,—"I am dying, Egypt"—when rugged men who ruled the world tumbled from glory to a gory grave—because a Cleopatra knew her cosmetics better than the Caesars knew their strength.

Remember too the Pompadours, Dubarrys, Gwynnes and Borgias—the Jezebels, and Shebas, the good queen Bess with ruffled dress and face of kalsomine—how well they ruled their day and age because they ruled their men. But antiquity does not justify iniquity—and beauty and goodness today go commonly hand in hand.

For the Cosmetic urge in the bad old days was only for the classes, and the masses were still unwashed and unrefined.

Today, however, there is a real democracy of beauty seekers, especially in our country where mill dolls and dowagers, girls of ten and mothers of ten, vie with each other in search of new charm—and the supplying of materials to furnish this dubious performance now stands as one of the nation's leading industries.

The Cosmetic splurge *ranks* (!) third in advertising expenditures, if that be any criterion of the extent of the business.

A wag has suggested for the industry's slogan,—“Women can't go wan forever”—and the industry certainly does its share to keep them gay and colorful.

And while there are those who deplore this pretty business and regard it as a passing, foolish fad—it has merits well worth holding.

Someone has said that “the use of cosmetics is not a moral question, but a restorative art.”

Everyone cannot lay claim to visible beauty—but everyone should be as beautiful as possible, if only for the eye ease of others.

And the *regulated* and *responsible* manufacture of cosmetics has every right and claim to be regarded as a serious, serviceable business.

IVOR GRIFFITH.

Diodrast

3,5-diiodo-4-pyridone-*N*-acetic acid and diethanolamine.— $C_5H_2ONI_2 \cdot CH_2 \cdot COOH + NH(CH_2CH_2OH)_2$.—A mixture or a loose combination (in solution) of diethanolamine, $NH(CH_2CH_2OH)_2$ and 3,5 diiodo-4-pyridone-*N*-acetic acid, $C_5H_2OHNI_2CH_2 \cdot COOH$ in equimolecular quantities. Diodrast contains approximately 49.8 per cent. of iodine.

Actions and Uses—Diodrast is proposed as a contrast agent for intravenous urography.

Dosage—Twenty cc. of a solution containing 7 gm. of diodrast, previously warmed to body temperature, is injected slowly, usually into the cubital vein. Children are given correspondingly smaller doses. Diodrast is administered intravenously in the form of an aqueous solution; each cubic centimeter contains 0.35 gm.

It is manufactured by Winthrop Chemical Company, New York.

SELECTED EDITORIAL

INVESTING TIME

ONE of the few departments of the United States Government which shows a profit is the Philatelic Agency. This Agency, created within recent years, owes its existence to the demands of stamp collectors, whose purchases from the Agency alone are currently at the rate of \$1,000,000 a year. This figure, and the fact that it has been increasing steadily, regardless of the trend of general business, attests the importance of stamp collecting as a hobby. Such growth is, however, not confined to stamp collecting; hobbies of all sorts have been following the same trend.

Hobbies, generally, may be roughly classified as either collecting, or games and sports, or handicrafts, or study and research. Hobbies of a scientific and research nature are perhaps less common than those of other types, but they have very serious devotees in all walks of life. Many contributions of great importance to science have been made by such amateur investigators. One field in particular—that of radio communication—has to a notable extent been developed by amateurs, large numbers of whom, all over the world, have been building and improving circuits and studying transmission at various wave lengths, over a period which extends back many years before the first commercial broadcasting station (other than for code messages) was opened. Amateur astronomy is another hobby which has many adherents. Unlike radio, astronomy is an old science, but it has always had many contributors from the ranks of those who did not work at it as a means of making a living. In spite of its age as a science, there are plenty of astronomical facts which the amateur may assist in gathering—facts which would otherwise wait perhaps for many years before the regular observatories would ever have the time to determine them. Amateur astronomers are steadily making contributions to the study of such matters as variable stars, solar eclipses and new comets, and are also promoting considerably the art of making telescopes.

Geology and related sciences have their quota of amateur adherents. Many of these study and collect solely for the pure pleasure of reading the records of the rocks and other indicia of antiquity; they may make no contribution to the advancement of the science, although

they spread an appreciation of its significance and the work which it is doing—as do most amateurs in any field.

Chemistry and physics have few serious followers outside the ranks of those who pursue these sciences as professions. For one thing, research along these lines often requires a degree of training and experience not necessary for many of the more popular avocations; furthermore, the apparatus and supplies required are in many cases beyond the reach of most people. But though the entrance requirements may be high, due reward comes to him who makes a real contribution.

Those individuals who have a sufficiently large supply of funds are in the fortunate position of being able, at least to a certain extent, to multiply themselves in terms of the hobbies they pursue. Not only can they indulge personally in one or more, but they can, with their resources, engage, and perhaps personally direct, other individuals who perform the actual work involved in the line of endeavor undertaken. Extensive and valuable investigations can be carried out along perhaps several lines, thus multiplying the fields from which the individual derives interest and enjoyment. Geological and archeological expeditions, chemical and physical research, studies of the ethnology of remote tribes, and aeronautics are a few widely separated fields which would come under the classification just mentioned.

The growing interest in hobbies is attested by the increase in publications and exhibitions and associations relating to them. Although these are concerned for the most part with collection or game or sport hobbies, nevertheless, a significant number have to do with those relating to science or to the handicrafts. Exhibitions of non-collecting hobbies of members have been held by Brown University and by the American Society of Mechanical Engineers. Business men's clubs hold exhibitions of paintings and sculpture done by their members. Study of the general subject of use of leisure time is being made by the National Recreation Association and other organizations and individuals; study of the type of hobby followed by persons in each business or profession is going forward. While all these studies are, to a large extent, in their infancy, it is hoped that they will assist materially, as time goes on, in securing to every person the most intelligent and enjoyable use of his leisure.—(*Ind. Bull. A. D. Little, Inc.*)

ORIGINAL ARTICLES

STUDIES ON OIL OF TURPENTINE: CAMPHOR FROM PINENE-HYDROCHLORIDE

By W. E. Hanford and G. W. Perkins

(Contribution From Organic Chemistry Laboratory, Philadelphia College of Pharmacy and Science)

CAMPBOR has been an important ingredient of certain plastics for a number of years and domestic manufacturers were for some time dependent on foreign markets for their supply. We find in recent years however, a considerable tonnage production of synthetic camphor made from raw materials readily available in this country (1). We believe that as much encouragement as possible should be given to fostering of industries employing our natural resources and present herewith some studies that have been made on the synthesis of camphor, from a typical home product—turpentine.

The synthesis of camphor from oil of turpentine by the following steps: turpentine-pinene-pinenehydrochloride-camphene-bornyl-acetate-borneol-camphor, has been regularly assigned as a routine experiment to students taking extra work in organic chemistry, in this laboratory. From observations over several years it has been found that the largest loss in yield was in the step where pinene-hydrochloride was converted into camphene. The object of these studies was to increase the yield if possible, to study various patents and other methods for conducting this synthesis and to produce some original method if possible.

It has been found experimentally (2) that when pinene-hydrochloride is heated with sodium hydroxide for a number of hours, little reaction takes place and no borneol is formed. Other workers employing sodium stearate have been able to produce borneol from pinene-hydrochloride. Other salts like sodium benzoate and sodium acetate have been used, also sodium acetate (3) with excess of acetic acid. Berg (4) used sodium phenolate in the presence of an excess of phenol whereby steam distillation was made possible. This method was somewhat of an improvement over that of Reyhler (4) who used dry sodium phenolate. Bischler and Baselli (5) used lead, copper or manganese salts instead of the sodium salts of the higher fatty

acids and also added some diethylaniline, probably with the object of combining with any liberated acids. Their conversion was made at 195-200 degrees C.; and at atmospheric pressure.

Steiner (6) used salts of sulphonic acids and Billeter (7) modified Reychler's method by substituting a polyhydric alcohol, such as glycerin or carbohydrate as sugar and heated the pinene-hydrochloride with salts of these in the presence of water and under considerable pressure. We have made some study of this reaction. Other experimenters have tried to use amines and amides in order to bring about the conversion of pinene-hydrochloride to camphene but report little success. Weizmann (8) claims to have brought about the desired results by using heterocyclic bases of the pyridine group.

Dubosc (9) has brought about the removal of the hydrogen chloride by using a metal such as iron or zinc and a peroxide, such as barium peroxide or manganese dioxide. The pinene-hydrochloride is heated with a mixture of a peroxide and a metal for twenty-four to thirty-six hours, at the end of which time the conversion is complete. Montaland (10) used aluminum oxide and similar compounds to catalytically remove haloid acid. Similarly Schmitz and Stalman (11) have worked out a process employing alkali metal oxides and water to remove the hydrogen chloride.

Wesson (12) claims that by using a mixture of pinene-hydrochloride and glacial acetic acid in the presence of a 2 to 5 per cent. granular zinc, a high yield of products can be obtained which are convertible into camphor and that there is less resin formed than in any of the other processes where pinene-hydrochloride is changed into camphene and isobornyl acetate. He claims only 5 per cent. resin formation. Wesson further claims that the hydrochloric acid (gas) can be re-employed to produce more pinene-hydrochloride.

Hesse (2) reported that ethyl magnesium bromide accelerated the reaction between magnesium and pinene-hydrochloride. This has also been studied and will be discussed later. No reference was found to the application of the Friedel-Craft reaction to pinene-hydrochloride, hence this has also been studied and will be discussed later.

Experimental

Excellent methods for preparing pinene-hydrochloride are described in certain laboratory manuals of organic chemistry (13). The pinene-hydrochloride used in these experiments was made as follows: Mix 500 grams of oil of turpentine with 5 grams of clean sodium

in a liter flask, attach a fractionating column and distil. Adjust the temperature so that gentle boiling takes place with total reflux for about ten minutes, then increase temperature and distil and collect fraction from 154-160 degrees C. Almost any type fractionating column is satisfactory, we have used a three-bulb Glinsky column and various type packed Hempel columns. The rectified turpentine is principally alpha-pinene. The pinene obtained above is placed in a bottle of suitable capacity (about 800 cc.) with a wide mouth sufficiently large enough so that the stopper may be bored and provided with an inlet tube reaching nearly to the bottom, and outlet tube fitted with a calcium chloride drying tube, a stirrer with mercury seal and a thermometer. Wide mouth bottles such as chemicals are packed in are suitable for use. The bottle is set up in an ice bath and when the temperature of the pinene reaches 5 degrees C. dry hydrogen chloride is passed through the pinene at such a rate that the temperature does not rise above 15 degrees C. Better yields are obtained when the temperature is kept near to 5 degrees C. The hydrogen chloride gas must be thoroughly dried and suitably trapped to take care of any back pressures. The gas is readily absorbed by the pinene and near the limit of absorption the liquid becomes pasty. This depends however on how closely the temperature is regulated and cannot be taken as a criterion. When the gas is no longer absorbed the liquid is cooled below 0 degrees C. and the crystalline pinene-hydrochloride filtered off. A second crop of crystals can be obtained by saturating with more gas and chilling. The pinene-hydrochloride obtained in this way is of good quality and camphoraceous odor.

EXPERIMENT NO. I

Thirty grams of pinene-hydrochloride, 50 grams of glacial acetic acid and 16.8 grams of anhydrous sodium acetate were placed in an acetylation flask and the material heated on a sand bath at as rapid a reflux as possible without loss of acid, for a period of seven hours. After cooling the material it set to a solid mass to which was added about 100 cc. of water and then warmed until the oil floated freely on the surface of the solution. On cooling a tan colored semi-solid separated out from which the aqueous acid solution was decanted. The material was warmed and a solution of sodium carbonate added until neutral. The aqueous layer was again separated by decantation after cooling. The material was then filtered and washed free from

sodium carbonate and allowed to dry in a vacuum desiccator over night. A saponification analysis on this material and calculated to bornyl acetate was only 4.6 per cent. yield.

EXPERIMENT No. 2

Twenty-eight grams of pinene-hydrochloride, 56 grams of glacial acetic acid and 24.5 grams of anhydrous sodium acetate were used in repeating the procedure of No. 1. Saponification analysis on final product showed 4.5 per cent. of bornyl acetate.

EXPERIMENT No. 3 (9)

One hundred grams of pinene-hydrochloride, 21 grams of finely divided iron and 33 grams of manganese dioxide were placed in a liter balloon flask, attached to an air condenser and the material heated for fifty hours at such a temperature that the material refluxes about halfway up the condenser. When the material had cooled about 250 cc. of water were added and the material steam distilled. The oily material was separated from the aqueous layer. The weight of the oily material was 25 grams. No camphene could be extracted from this oil by freezing out or by distillation. The liquid distilled above 160 degrees C.

EXPERIMENT No. 4 (7)

Thirty-four grams of lime, 69 grams of sucrose, 69 grams of pinene-hydrochloride and 100 grams of water were mixed thoroughly in a mortar and the mixture added to an autoclave. The material was then heated until about 140 pounds gauge pressure was recorded, corresponding to a temperature of approximately 170 degrees C. The material was heated for nine hours and on cooling was placed in a flask and steam distilled. The distillate was oily and had a pine-like odor, and the yield was 33 grams. Refractive index at 22 degrees C. was 1.7412. Specific gravity of the oil at 20 degrees C. was 0.9268. The oil had a boiling range of 163 to 193 degrees C. The largest part of the distillate being collected from 163 to 172 degrees C. An attempt was made to vacuum distil at 20 mm. pressure but the material exhibited violent bumping even when an air leak was used. As some of the material flowed down the condenser, small crystals were observed on the side of the tube, so the material was separated by placing the oil in an ice and acid mixture and the crystals filtered off. The few crystals obtained had a boiling point only 2 or 3 degrees above that of camphene. This substance was produced in such

small amount that insufficient material was had for further purification.

EXPERIMENT No. 5 (2)

Seven and one-half grams of magnesium were placed in a dry flask fitted with a reflux condenser and separatory funnel. Ten cc. of dry ether was added followed by 3 cc. of ethyl bromide and a crystal of iodine. Ethyl magnesium bromide was formed and when the reaction had nearly ceased, 15 more cc. of dry ether were added and then a solution of 50 grams of pinene-hydrochloride dissolved in 25 cc. of dry ether was slowly added. When all reaction had ceased the flask was heated on a water bath for two hours, then 44 grams of camphor dissolved in 80 cc. of dry ether was slowly added and the material heated for two more hours on a water bath after the addition of the last portion of the camphor solution. The mixture was then made acid with dilute hydrochloric acid and the aqueous layer separated from the ether layer and the ether was treated with sodium carbonate to neutralize any free acid. The ether layer was again separated from the aqueous solution, treated with sodium sulphite to remove any free iodine and then washed with water. The ether was distilled off and the residue steam distilled. The material was crystallized from ether and weighed. The weight of the product thus obtained was 56.0 grams. A qualitative test for halogen showed the presence of considerable amount. The melting point of the material was over a range of 127-132 degrees C. which on further purification was found to be a mixture of camphor and pinene-hydrochloride. This demonstrated that the reaction between magnesium and pinene-hydrochloride is not complete. It was thought that a Grignard compound could be made from the pinene-hydrochloride which in turn could be coupled to the ketone group of camphor which product could then be oxidized to form two molecules of camphor.

This experiment was repeated using ammonia gas at the end of the experiment but negative results were also obtained. (Experiment No. 6.)

EXPERIMENT No. 7

Considering the position of the chlorine atom in pinene-hydrochloride it was thought that this chlorine might be active enough to respond to a Friedel-Craft reaction, whereby the chlorine could be replaced by a group which could be subsequently split off. One hun-

dred and fifty cc. of carbon disulphide were placed in a liter balloon flask, 50 grams of pinene-hydrochloride, 40 grams of anhydrous aluminum chloride were added and the flask attached to a reflux condenser. Glacial acetic acid was slowly added through the condenser. A violent reaction took place and the mass turned an orange red color. On addition of more acetic acid the material became a very dark greenish black. When the reaction had stopped, the material was heated for several hours and then the excess of carbon disulphide was distilled off and the green semi-solid mass was subjected to steam distillation. A white solid was obtained which was dissolved in ether, separated from the water, washed with sodium carbonate and the ether layer evaporated. A saponification with alcoholic potassium hydroxide was made with a known weight of sample but showed only the presence of traces of saponifiable matter. The melting point of the mass was over a range of 93 to 97 degrees C. After redistillation at 15 mm. pressure the distillate so obtained on cooling gave a solid with a melting point range 72 to 75 degrees C. The non-steam distillable material was of a dark reddish brown color and possessed an odor similar to that of organic sulphur compounds. The yield of final product in this experiment was 12 grams.

EXPERIMENT No. 8

Fifty grams of pinene-hydrochloride were dissolved in 200 cc. of petroleum ether and placed in a one-liter balloon flask, 30 grams of aluminum chloride were added and the flask attached to a reflux condenser through which 30 grams of glacial acetic acid were slowly added. A rose-colored solution was formed at first which later turned to a pale violet. After the mixture had stood for twenty-four hours with occasional shaking, 15 grams more of aluminum chloride were added and the mixture allowed to stand for five hours. The petroleum ether was then distilled off and the residue subjected to steam distillation. The steam distillate was treated as given under previous experiment except that petroleum ether was used instead of ether. The results of the saponification of the material formed showed an ester figure which calculated to 10.3 per cent. yield of bornyl acetate. There was still a large percentage of the pinene-hydrochloride unchanged as shown by qualitative test for halogen. The melting point of the purified material was 74 degrees C. The yield of material from the steam distillation was 33.5 grams.

EXPERIMENT No. 9

The above experiment was repeated using kerosene as a solvent. The solution developed a deep violet color. It was found to be practically impossible to separate the products formed in this run from the solvent used.

EXPERIMENT No. 10

Anhydrous zinc chloride was used in place of aluminum chloride in repeating the procedure followed in No. 8. It was found necessary to use heat to start the reaction in this case. The results of the saponification of final product showed a yield of 8.6 per cent. of bornyl acetate. The melting point range of the material was 60 to 85 degrees C. The percentage of tarry residues in this run was much lower than in the previous ones.

Summary

1. Pinene-hydrochloride (sometimes known as bornyl chloride) may be easily and conveniently prepared from alpha-pinene, but in order to secure maximum yields; the pinene used must be of high quality, the hydrogen chloride must be anhydrous since even traces of water seem to lower the yield, the temperature of the pinene during the addition of the hydrogen chloride must be carefully maintained at 5 degrees C.
2. When salts of fatty acids such as sodium acetate are used to remove the halogen from pinene-hydrochloride, yields of bornyl acetate are not increased with increase of sodium acetate.
3. Halogen may be removed from pinene-hydrochloride in aqueous solution under pressure by means of lime and a carbohydrate.
4. Pinene-hydrochloride was not found to be reactive to magnesium under the conditions of the experiment and catalyst used.
5. The application of the Friedel-Craft reaction to formation of camphor derivatives from pinene-hydrochloride is believed to be new and shows promising results which will be further studied.
6. Most of the methods reported applicable for removal of halogen from pinene-hydrochloride gave tarry residues that are difficult to separate.

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**Mme. Curie, Co-discoverer of Radium—Long an Honorary
Member of the College**

The death of Mme. Curie recalls an early recognition of her scientific achievements by the Philadelphia College of Pharmacy and Science, whose members, in 1909, elected her an honorary member of the college.

A letter of appreciation, in Mme. Curie's handwriting, is hanging in the president's office in the college building. The English translation follows:

"Paris, October 26th, 1909.

Mr. Secretary.

I pray you to kindly transmit to the assembly of the members of the Phila. College of Pharmacy my sincere thanks for the honor which they conferred upon me in naming me an honorary member.

I pray you to accept my sincere salutations and the assurance of my sentiments.

M. CURIE.

Professor of the Faculty of Science of Paris.

To the Secretary of the College of Pharmacy of Phila.

Very truly,

A. W. MILLER."

SURFACE TENSION DETERMINATIONS OF SOME BARBITURATES*

By J. Howard Graham

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BARBITURIC ACID is the mother substance of over five hundred preparations,(6) several of which are well-known hypnotics. About one hundred of these latter have been made in pharmaceutical laboratories and research with them has been very active chemically and biologically during recent years. Every now and then the pharmacist has his attention drawn to derivatives for which new and better claims are made and he does not always understand the basis for these. Claims are made about "lowered surface tension" and labeled for instance, "S. T." of "S. T. 37". The writer, while interested in this property, recently made a study of the lowering of surface tension of water by the presence of certain barbituric acid derivatives, some of which he purchased in the open market, some of which he prepared in the laboratory. The purpose of this paper is to explain surface tension briefly; to cite instances where it is believed it plays an important role; and to give numerical data, obtained by experiment and representing some of regular laboratory work of his students in physics.

SURFACE TENSION: For the immediate discussion of it we are concerned only as it relates to the liquid and gaseous phases. At the surface of a liquid, where it comes into contact with air, the molecules are arranged in a more orderly fashion than are the other molecules of the liquid. The least active parts of the molecules, or the least polar groups as they are termed, are oriented toward the vapor phase. In 1917, (1) it was pointed out that with organic paraffin derivatives, the CH_3 groups turn outward; and more active groups, such as NO_2 , COOH , NH_2 , OH and numerous others, or, groups which contain N, S, O, I, or double bonds, turn toward the interior of the liquid. The orientation of the molecules of hexyl alcohol are often represented in drawings, as black pins with their heads down in the liquid and the points up in the air. The heads of the pins represent the OH groups, the most active part of the molecule. Surface tension of a liquid is defined as the number of dynes of force necessary to pull apart those molecules of the liquid surface which border an imaginary line one

*Read at the Fifty-seventh Annual Meeting of Pennsylvania Pharmaceutical Association, June 21, 1934.

centimeter long, and a dyne is that force which will impart to one gram of mass an acceleration of one centimeter per second. Some phenomena which are of common observation and which depend upon the surface tension of water, are floating steel needles, motions of water bugs over the surface, distention of films of soap-bubbles, detergent actions of various cleansers, separation of valuable ore from gangue by oil flotation, etc. Of three methods frequently used to determine surface tension, our laboratory uses that of DuNouy, with his precision type of tensiometer, the operations demanding extreme cleanliness from grease and dust.

SURFACE TENSION IN BIOLOGY: Perhaps the complete biologic action and value of surface tension will never be understood fully but research is active along these lines today so we will enumerate some of its findings taken from recent literature. As concerning the relation of antiseptic action to surface tension, it is stated (2) that of the three isomeric nitro β amino ethylaminoquinolines, the 8-nitro-7 β aminoethylaminoquinoline has very little antiseptic properties and does not lower the surface tension of water. The 5-nitro-8 β derivative inhibits the growth of *E. coli* and *St. aureus* in 1:1000 solution; and in 1 per cent. solution lowers the surface tension of water 16 dynes. The 8-nitro-5 β isomer has intermediate properties.

In an excellent French paper (3) on the role of surface tension in biology, it is convincingly stated that surface tension plays an important part in the phenomena of immunity; that phenomena of cytolysis and of hemolysis may be characterized by a significant lessening of the surface tension, and that modifications of surface tension may accompany the mechanism of the Wassermann reaction.

It was shown in 1919-20 that the serum of syphilis is plainly labilized and that this labilization is brought about by the inversion of the electric charge of certain serum colloids, by an increase of the surface tension. Again, there are reasons for believing that modifications of surface tension occur in the media of culture of various microorganisms and that microbic antagonism can perhaps be explained by variations of this constant in two opposite directions. It holds in particular for the antagonisms between the pathogenic microbes and the saprophytes. Several thousands of measurements have demonstrated that the surface tensions of organic liquids (serums, liquids and spinal fluids) and particularly of animal serums, are fixed. The fixity of the surface tensions are possible, thanks to the existence

of efficient special regulators, which we have scarcely begun to understand. While the mechanism of regulation remains intact, no modification of the physical or physico-chemical character of the blood can take place, but once this mechanism is changed, the modifications in question appear. The buffer power of the blood reflects the whole tone of the organism. Nevertheless when this buffer power is exhausted, the surface tension can be modified, as has been observed in serious cases of syphilis (Lunz), of T. B. (Lunz) and above all, in cancer (Bauer and others). Another medical application worthy of mention is, that minute quantities of bile salts can be detected in urine (Hay) by a marked lowering of the surface tension.(3)

THE BARBITURATES: Within comparatively recent years, members of the barbituric acid family have come into prominence as hypnotics, in routine medical practice, pre-anesthetic sedation, and for the prevention of local anesthetic reactions. In a recent study by Tabern and Shelberg (4) of the relation of the physical chemical properties to hypnotic action, they refer to Traube (5) as suggesting that the surface tension of the hypnotic solution may be the deciding factor in determining its efficiency. Referring to a recently revived theory of Bernard by Bancroft and Richter (5) with evidence presented that hypnosis is in most instances associated with reversible coagulation of cell colloids, Tabern and Shelberg state, "Coagulation may be the mode of action within the cell, but there remains in clinical practice the all-important necessity for transporting the hypnotic from the point of administration to the interior of the cell through a series of transferences. Here, surface tension, absorption and more particularly lipid solubility appear to be the limiting factors in the chain of events." The work of these investigators seems to substantiate this finding. They have based their comments upon experimentation with fifteen barbiturates of known efficiency rating.

As to our own surface tension determinations, made with the DuNouy Precision Tensiometer, between temperatures of 28 and 29 degrees C. and upon freshly prepared solutions of concentration 1:1250 the first five barbiturates having been made in the school laboratories, results are obtained which will compare quite well with results obtained by others in relation to their efficiency ratings as hypnotics.

Five determinations (closely agreeing) were made in each case, with the average recorded in the table. Nembutal (so introduced) was taken from a capsule, while Pentobarbital (the same barbiturate) was taken from an ampule. Results are expressed as percentages of the normal value for water taken at the same temperature.

<i>Water and the Barbiturates</i>	<i>S. T. Average</i>	<i>Per Cent. S. T. Con. 1:1250</i>
Water	72.78	100.
Barbituric acid	72.64	99.7
Barbital (Veronal)	72.22	99.1
Barbital (Na.)	72.40	99.5
Thiobarbital	71.38	97.9
Thiobarbital (Na.)	71.96	98.7
Nembutal (Na.)	70.64	96.9
Pentobarbital (Na.)	69.38	95.2
Amytal	61.36	84.3
Amytal (Na.)	69.26	95.0
Phenobarbital	71.84	98.6
Phenobarbital (Na.)	72.54	99.5
Ortal (Na.)	53.06	72.9

Note how the sodium salt has a higher value than the corresponding substituted barbituric acid.

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REPORT OF THE COMMITTEE ON DRUG MARKET
of the
PENNSYLVANIA PHARMACEUTICAL ASSOCIATION

THE report of the Committee on Drug Market is mainly a survey of the field concerning the quality of medicinal products and is directed exclusively to items which have come under the supervision of members of the committee. As a consequence we are able to give accurate and first hand information concerning the quality of the material considered in our report, which covers a wide field, containing items examined by consulting, pharmaceutical and wholesale drug laboratories.

Our analyses of the thousands of items conducted under the supervision of the members of the committee show that there is not one instance of intentional fraud or substitution. All of the rejected goods were refused because of poor quality. Some were only slightly sub-normal but several were decidedly unfit. On the whole, the standard of quality is very high. Commenting on this phase, R. I. Grantham states that the number of items rejected in proportion to the total number examined is quite low and that the trade is receiving very high grade material. He also brings out the fact that the knowledge among shippers that the goods are to be tested is instrumental in maintaining quality.

Among the chemicals we find that arsenous iodide, carbon tetrachloride, lime, magnesium carbonate, calcium lactate and sodium phosphate were not of U. S. P. quality. Mercury with chalk contained an excess of mercury oxide, codeine phosphate had an excess of insoluble foreign matter technically known as "floaters", and two shipments of potassium alum contained ammonia. One shipment of tetrachlorethylene had an abnormal boiling point and an excess of carbonizable impurities, and three lots of sodium chloride did not comply with the specifications for chemically pure products. Boric acid contained an excessive amount of insoluble substances, and iron phosphate precipitated an excess of ferric iron. One lot of amidopyrine had an undesirable yellow color.

Of the many samples of volatile oils examined, one sample of oil of rosemary, one of oil of lavender and one of oil of peppermint did not comply with the requirements of the U. S. P. Another sample of oil of peppermint was unsatisfactory because it did not meet

private specifications. Two carboys of a five-carboy shipment and one carboy of another five-carboy shipment of ammonia water 26 degrees were found to be of sub-standard quality. One drum of 20 degrees ammonia water contained an excess of insoluble matter.

An excessive amount of foreign matter was found in a lot of tolu, and an offering of extract of witch hazel was contaminated with copper. One lot of caramel was low in color value. Another lot yielded a precipitate in 68.5 per cent. alcohol instead of remaining clear until the alcohol content had reached 80 per cent.

The following table of spices, submitted by the LaWall & Harrison laboratory, is offered for reference purposes and is of value in the study of the relative proportions of the various constituents of spices.

		Spices			
		Ash	Acid Insoluble Ash	Non-Volatile Ether Extract	Volatile Ether Extract
Allspice		4.25 per cent.	0.30 per cent.	7.60 per cent.	
Cinnamon		4.40 " "	0.75 " "	2.8 " "	
		5.27 " "	0.45 " "	4.25 " "	3.00 per cent.
		4.36 " "	0.43 " "	2.49 " "	2.66 " "
		5.50 " "	0.55 " "	3.80 " "	3.75 " "
		4.25 " "	0.45 " "	1.90 " "	3.20 " "
		4.65 " "	0.45 " "	2.45 " "	2.40 " "
		4.80 " "	0.55 " "	2.30 " "	3.05 " "
		4.90 " "	0.65 " "	5.00 " "	2.80 " "
		4.75 " "	0.55 " "	1.80 " "	4.90 " "
		4.50 " "	0.55 " "	3.60 " "	3.30 " "
	Max.	5.50 " "	0.75 " "	5.00 " "	4.90 " "
	Min.	4.25 " "	0.43 " "	1.80 " "	2.40 " "
Cloves		6.60 " "	0.40 " "	7.85 " "	17.50 " "
		6.37 " "	0.17 " "	7.26 " "	19.0 " "
		6.32 " "	0.10 " "	6.25 " "	20.50 " "
		6.30 " "	0.35 " "	7.45 " "	21.55 " "
		6.40 " "	0.45 " "	7.05 " "	19.55 " "
	Max.	6.60 " "	0.45 " "	7.85 " "	21.55 " "
	Min.	6.30 " "	0.10 " "	6.25 " "	17.50 " "
Mace		2.20 " "	0.275 " "	29.50 " "	
		2.50 " "	0.47 " "	29.20 " "	
		2.00 " "	0.15 " "	29.95 " "	
		2.50 " "	0.35 " "	29.05 " "	
		2.82 " "	0.40 " "	29.25 " "	

		Ash	Acid Insoluble Ash	Non-Volatile Ether Extract	Volatile Ether Extract
		2.75	" " 0.35	" " 28.10	" "
		2.75	" " 0.37	" " 29.05	" "
		2.75	" " 0.40	" " 29.55	" "
		2.75	" " 0.35	" " 29.90	" "
		2.70	" " 0.30	" " 29.05	" "
		2.85	" " 0.30	" " 28.00	" "
		2.95	" " 0.40	" " 29.15	" "
		2.70	" " 0.30	" " 29.05	" "
		2.95	" " 0.25	" " 24.90	" "
		2.85	" " 0.50	" " 28.45	" "
	Max.	2.95	" " 0.50	" " 29.95	" "
	Min.	2.20	" " 0.15	" " 24.90	" "
Nutmeg		2.00	" " 0.45	" " 39.95	" "
		1.8	" " 0.05	" " 37.35	" "
Pepper		5.10	" " 0.60	" " 7.75	" "
		6.30	" " 1.10	" " 7.95	" "
		4.65	" " 0.55	" " 9.95	" "
		4.50	" " 0.55	" " 9.45	" "
		4.85	" " 0.60	" " 10.40	" "
		4.95	" " 0.55	" " 9.65	" "
	Max.	6.30	" " 1.10	" " 10.40	" "
	Min.	4.50	" " 0.55	" " 7.75	" "
Pepper, Cayenne		6.03	" " 0.65	" " 18.60	" "
		6.40	" " 0.60	" " 15.00	" "
		6.85	" " 0.60	" " 15.90	" "
		5.20	" " 0.50	" " 18.00	" "
	Max.	6.85	" " 0.65	" " 18.60	" "
	Min.	5.20	" " 0.50	" " 15.00	" "
Pepper, White		1.25	" " 0.18	" " 7.65	" "
		0.85	" " 0.05	" " 7.65	" "
		1.00	" " 0.30	" " 8.60	" "
		1.15	" " 0.10	" " 7.25	" "
		1.20	" " 0.30	" " 8.60	" "
	Max.	1.25	" " 0.30	" " 8.60	" "
	Min.	0.85	" " 0.05	" " 7.25	" "
Pepper, Red		5.72	" " 0.35	" " 13.45	" "
		6.15	" " 0.90	" " 16.70	" "
		6.25	" " 1.0	" " 16.90	" "
	Max.	6.25	" " 1.0	" " 16.90	" "
	Min.	5.72	" " 0.35	" " 13.45	" "
Pepper, Black		5.25	" " 1.15	" " 8.75	" "
Coriander,		6.10	" " 0.32	" " 20.95	" "

		Ash		Acid Insoluble		Non-Volatile Ether Extract		Volatile Ether Extract
Ground		6.5	" "	0.35	" "	20.95	" "	
		6.60	" "	0.6	" "	20.40	" "	0.50 per cent.
	Max.	6.60	" "	0.6	" "	20.95	" "	
	Min.	6.10	" "	0.32	" "	20.40	" "	
Marjoram		12.0	" "	3.5	" "			

		Acid Insoluble	Water Insoluble	Water Soluble	Cold Water Extract	Calcium Oxide	Crude Fibre
Ginger	Ash	Ash	Ash	Ash	Extract		
	3.97	0.40	1.27	2.70	14.10	0.137	3.60
	4.85	0.35	1.35	3.50	14.60	0.229	3.50
	4.90	0.55	2.40	2.00	14.10	0.442	4.00
	4.92	0.22	1.42	3.50	13.50	0.458	4.60
	3.5	0.15	1.05	2.45	16.20	0.156	4.10
	4.65	0.30	1.65	3.00	12.60	0.207	4.75
	4.50	0.22	1.95	2.55	13.00	0.292	4.60
	4.50	0.30	1.90	2.60	13.50	0.222	4.75
	3.85	0.20	1.45	2.40	16.20	0.222	4.85
	5.98	0.58	3.38	2.60	13.60	0.638	5.90
	Max. 5.98	0.58	3.38	3.50	16.20	0.638	5.90
	Min. 3.50	0.15	1.05	2.00	12.60	0.137	3.50

Crude drugs are more likely to be of sub-standard quality than other classes of medicinal products, as they are more subject to climatic conditions and natural deterioration. Unavoidable contamination with moderate amounts of other parts of the plant or even small quantities of unavoidable earthy material clinging to hairy leaves or roots is excusable, but the offering of what the United States Department of Agriculture considers "filthy" material is unwarranted. Recent rejections of this class of goods included anise, caraway and cumin seeds.

Careless gathering is responsible for many rejections as shown by shipments of catnip herb, pennyroyal leaves and cubeb berries because of the presence of an excess of stems. Two instances of improperly prepared or gathered material are shown in powdered turmeric root which was too light in color, and a shipment of Hungarian chamomile flowers which were too dark in color. A case of careless preparation of material is that of a shipment of ground white oak bark which had a very pungent odor somewhat like pepper

probably due to the fact that the mills were not properly cleaned before grinding the material. Good quality fennel seed is extremely difficult to obtain at the present time as most of the goods on the market are old crop and brownish in color. Satisfactorily clean stramonium leaves are difficult to obtain because the hairy nature of the leaves retains any earthy material with which they come in contact. Two lots were rejected for this reason, as shown by an excess of acid insoluble ash. The nearest approach to adulteration was a lot of cudbear which contained starch.

The U. S. Department of Agriculture, Bureau of Chemistry, which has jurisdiction over imports, is responsible for many rejections. Recently they detained shipments of twenty-five bales of belladonna leaves, twenty-six bags of coriander seed, 200 bags of cumin seed, and forty cases of mace, because the goods did not conform to the proper standards.

Among the physiologically tested drugs, we find that all samples of digitalis leaves and both Spanish and Russian ergot were of good quality. Most of the red squill showed a M. L. D. below that required for squill when tested on albino rats.

Submitted to the fifty-seventh annual meeting of the Pennsylvania Pharmaceutical Association, Wernersville, Pa., June 19, 1934.

J. G. ROBERTS, *Chairman*,
JOS. W. E. HARRISSON,
R. I. GRANTHAM,
J. MERVIN ROSENBERGER.

THE PHYSICIAN AND THE PHARMACIST OF TODAY*

By Mitchell Bernstein, M. D., P. D.
Philadelphia

IN THESE changing times, it is but natural that the professions of Medicine and Pharmacy should be affected either directly or indirectly. Aside from the consideration of the economic phases, there have been vast changes within the professions from the scientific standpoint. It is with the effect of these changes that we are directly concerned at the moment, especially as they apply to practicing physicians and pharmacists.

At once we are met with the fact that the prerequisite requirements for entering either profession are higher today than ever before. The undergraduate courses in pharmacy have been advanced to four years of study, while the medical student is compelled to serve an internship of at least one year in a recognized hospital subsequent to graduation from a medical college. After the foregoing preparation, the graduate in pharmacy or medicine of today is equipped to enter the practice of his respective profession.

The modern graduate in pharmacy enters his profession having at his command the advantage of all the recent scientific progress, be it chemical, bacteriological, pharmaceutical or biological. In medicine, he has the advantage of the most recent work in any one of the various phases of this broad study. Because of this knowledge, it would seem that the opportunity of the young graduate of today for success is greater than that of his colleagues of previous years who may lack the knowledge of the recent advances in their respective fields.

True, the many years of experience are a great advantage to the senior brother in establishing prestige and a worldly viewpoint. But this apparently is insufficient to meet the rapid tide and undercurrent of the junior members of the professions, equipped with their present-day scientific background.

The problem then naturally arises as to what the pharmacists or the physicians who have been out of college for some years must do to march shoulder to shoulder in the professions with their younger colleagues.

*Read at the Fifty-seventh Annual Meeting of the Pennsylvania Pharmaceutical Association, Wernersville, Pennsylvania, June 20, 1934.

In medicine, specialization has developed to such a degree that it is a very difficult task for the physician engaged in general practice of medicine to keep abreast with the advances in all the various specialties. However, in a general way, familiarity with the advances in medicine must be readily acquired and assimilated as they occur and are applicable to the practice of medicine in a broad sense. Thus the chemical study of the blood for sugar, urea, creatinine, phosphorus, calcium, carbon dioxide, etc., in both health and disease, yields facts with which every modern physician must be familiar. If he is not, he finds himself in difficulties sooner or later. The Roentgen ray, the electro-cardiograph, basal metabolism study, modern microscopic study of the blood, the bacteriological study of the causation of various diseases, advances in physiology and pathology of the glands of internal secretion, the importance of the vitamins, and many other scientific advances, have all served to influence the medical thought of today. Teachers in medicine, of necessity, have had to keep abreast with the researches in the laboratory. The wide-awake, up-to-date physician has been forced to familiarize himself with each change in scientific trends, their interpretation and significance. This, of course, often is very difficult and obviously requires hours of study, reading, attendance upon medical meetings, free association with the men who are writing, teaching, and taking part in the forward march of medical science. There is no doubt that it may seem discouraging to be compelled to change one's scientific viewpoint a few years after graduation from college, yet progress of science necessitates it.

Years ago the practice of medicine was largely based on the belief chiefly gained by bedside experience, but often not substantiated by laboratory investigation, which is of our own era. Scientific investigation has yielded the causes of many diseases together with an understanding of their effects and hence there has been established a rational basis for the scientific treatment and management of the sick. True, this is not so for all the ills to which flesh is heir, but even in those without ascertained causation, progress has been made.

Today when a patient complains of a headache, he is subjected to a study of his entire body, because it is known that this symptom alone can be caused by unaccountable diseases, varying from rhinitis to brain tumor. Before a modern physician prescribes phenacetine of the United States Pharmacopœia, for a headache, he is compelled to make a searching investigation of the patient's head, eyes, chest, heart,

blood vessels, abdomen, and in fact the entire body. In addition, further investigations are often necessary including blood chemistry, urine study, and perhaps several X-rays. After all of this, the physician can prescribe intelligently for the patient's headache, which in the final analysis may prove to be only functional in nature and not organic.

Pharmacists likewise have been compelled to meet the newer scientific changes. Modern medical discoveries have forced upon the pharmacist the necessity for an understanding of the newer *materia medica*. The galenicals of old with few exceptions are gradually being pushed aside. In their place one sees an avalanche of coal tar derivatives and chemical compounds of various combinations. Advances in endocrinology have forced upon the pharmaceutical profession a list of endocrines such as pituitary products, ovarian, thymic, thyroid, and many similar preparations. The discovery of insulin by Banting for the treatment of diabetes, parathormone for the treatment of tetany, only to mention these as illustrative of a large group of valuable and indispensable remedies, has brought into bold relief the necessity for the large pharmaceutical manufacturers. True, the various sera as diphtheria antitoxin, tetanus antitoxin, and others, have been produced by the large pharmaceutical houses for some time. Today, more than ever before, these large manufacturers are apparently displacing the retail pharmacist in so far as the manufacture of pharmaceutical preparations of the foregoing type is concerned.

Every one knows that it is time-consuming, expensive, and often impractical for a retail pharmacist to attempt to standardize preparations such as digitalis, suprarenal, etc. The retail pharmacist is obliged to shift such obligations and responsibilities to the manufacturing pharmacists, who in many instances are meeting this obligation excellently. These changes, in the progress of pharmacy are definitely here to stay and naturally they have forced upon the retail pharmacist a changed point of view.

Some pharmacists have become discouraged with these changing conditions and they are leaning to the various side lines of the drug store for an existence. They lament the loss of the prescription work from physicians and in many instances have threatened to discontinue their prescription departments. On the other hand, a few wide-awake and up-to-date pharmacists have seen an opportunity for encouraging strictly scientific pharmacies. This line of cleavage between the vari-

ous types of pharmacists and pharmacies will undoubtedly become more marked as time goes on.

I believe that scientific pharmacy can do a great deal to help itself. It is not an exaggeration to say that only few pharmacists today are equipped to give physicians first-hand information regarding the newer *materia medica*. Where should the physician turn when he is eager for information concerning a new useful remedy official or otherwise: When the physician desires to know the comparative value of the various advertised digitalis preparations in relation to the United States Pharmacopoeia digitalis preparations, should not the pharmacist be the informant? Why should not the pharmacist make it his business to equip himself with the most recent list of new and non-official remedies, and have at his command all information regarding drugs pertaining to dosage, compatibilities, synonyms and the like, together with the comparative cost of trade-marked preparations and their United States Pharmacopoeia and N. F. equivalents. In addition, the pharmacist should have a weekly copy of the *Journal of the American Medical Association*, which gives a description of the new and non-official remedies as approved by the Council of Pharmacy of the American Medical Association.

May I add that the old-established pharmacist by constant reading of suitable medical and pharmaceutical journals and by attending pharmaceutical meetings, can gather a great deal of information that will be a liberal education in the scientific advances of his profession.

I believe that every up-to-date pharmacist equipped with this knowledge should devote some part of each day in detailing his local physicians, and so familiarize the physician with the fact that at the corner pharmacy is located the physician's most thorough therapeutic guide. The prescription department should be the rendezvous for the physician. Nearly all alert physicians make use of their pharmacists' scientific knowledge, but not all pharmacists appear to see the wisdom of impressing their scientific, specialized training upon their local physicians.

Radio broadcasting of subjects pertaining to health and disease is another problem that has come to influence both the practice of pharmacy and medicine as well as having a direct influence on the public health. Radio medical broadcasting serves a humanitarian purpose when it is supervised and is under the proper auspices of the legalized ethical medical and pharmaceutical societies or the health authorities

of the land. I must say that I am shocked at the inertia of the various legislative bodies of the country and the Congress of the United States in not arming the Federal Radio Commission with sufficient power to prevent the broadcasting day and night of an avalanche of radio medical "bunk."

Although some of the large pharmaceutical manufacturers are sincere in their broadcasting, making an effort to give the public the truthful and honest interpretation of the value of certain products, there are many who broadcast misleading statements without scientific accuracy.

This radio "bunk" is being broadcast to the gullible American public in the misbranded guise of scientific medicine. From toothpaste or mouthwashes, said to kill germs, without a qualifying statement as to the types of disease germs or a comparison with a scientific bacteriological standard, down to the so-called medicines to prevent children from catching colds, by taking a certain number of pills or pearls, the public is riddled with a babble that is both misleading and nauseating.

When an announcer or speaker over the radio states that this or that medicine is recommended by druggists, or is recommended by physicians, then unfair advantage is taken of the public, and gross misrepresentation is made of the medical and pharmaceutical professions, which, as professions, do not endorse such advertising.

The pharmacists' shelves are of necessity littered with thousands of dollars' worth of apparently useless remedies, the chief purpose of which is, apparently, easy money for the producers and profitable radio hours. Incalculable harm to human life is apparently being caused by this subtle quack medical advertising as long as this abuse is permitted to continue.

Through the heroic efforts of the late Dr. Harvey Wiley and the late President Theodore Roosevelt, the United States Food and Drug Act was enacted in 1906, and became effective January 1, 1907. This act was for the protection of the public against misbranding and adulteration of foods and drugs. Now the gullible public must be protected against an evil infinitely worse than food and drug alteration. Many sick could be cured of their ills, which may prove serious later, if they did not waste valuable time in self-medication at the solicitation of uncensored medical broadcasts. Victimized the sick should be curbed immediately.

The physicians and the pharmacists co-operatively should demand the regulation of medical broadcasts as a necessary public health measure.

May I say that the physician and the pharmacist of today should co-operate with each other to a greater extent than heretofore, for the mutual welfare of both professions which in turn would react to the general public good and welfare. The initiative for this co-operation could, to the best advantage of all concerned, originate in the camp of the profession of pharmacy, for after all the pharmacist is in a splendid position to inaugurate and supply such service to the physician.

Fly Sprays and Hay Fever

Dr. Kampmeier (*Jour. A. M. A.*, 1934, p. 205) has identified certain obscure protein idiosyncrasies as being due to fly sprays or wet and dry insecticides containing, or made from, pyrethrum. He concludes his remarks as follows:

"1. Pyrethrum, commonly used in insecticides, may cause hay fever and asthma.

"2. A patient may have coexistent sensitivity to this substance and to pollens of grasses and weeds.

"3. Exposure of such an individual to an insecticide containing pyrethrum may explain the apparent failure of desensitization for hay fever in a case theretofore successfully treated."

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Arthur Osol, Ph. D.

The Preparation of Sterile Solutions. H. Davis.* Bacteriological experiments have been made on a number of hypodermic injections showing the results obtained when solutions are prepared under normal conditions. It has been shown that, even in the presence of contamination much worse than that obtaining during any dispensing operations, sterile products can readily be obtained by exposure to streaming steam at atmospheric pressure for one hour. The instructions prescribed by the British Pharmacopœia for sterilization by Tyndallization are inadequate and sterility is not assured. When solutions are incubated during the intervals between successive heating, the nature of most of the common solutes is such that spores do not pass into the vegetative state and are consequently not destroyed when exposed to a temperature of 80 degrees C. and maintained at 80 degrees to 85 degrees C. for one hour on three successive days. The pH of a number of common hypodermic solutions has been determined before and after steaming for one hour and indications of decomposition of the solute are evidenced in certain cases. The sterilization of solutions of dextrose has been investigated and results suggest that concentrations in excess of 10 per cent. should not be sterilized by autoclaving at 10 pounds per square inch pressure. (From the Department of Bacteriology, University College Hospital Medical School.)

A New Method of Analysis of Some Mercurial Ointments. Wm. R. Heading.* The method recommended for the assay of mercury or one of its compounds in ointments, when it is distributed through, but not chemically combined with, the basis, consists of dissolving the basis in xylol in a centrifuge tube, and centrifugally separating the suspended solid. Most of the liquid is now syphoned off, and the process repeated twice with fresh portions of solvent, replacing the xylol after the first time with light petroleum. A layer of alcohol is now interposed between the deposited solid and the petroleum layer. The mixture is centrifuged again, and the petroleum layer, along with some of the alcohol, is drawn off. Either the res-

idual alcohol is now evaporated off, the solid dissolved in nitric acid, transferred to a flask and titrated with ammonium thiocyanate, or the mixture is shaken, the alcoholic suspension rinsed out into a flask, and the assay of the salt completed by the official or any suitable process. The method is suitable for any ointment in which the active constituent (1) has a specific gravity higher than that of light petroleum, (2) is not soluble in neutral organic solvents, (3) is not chemically combined with the ointment bases, (4) is capable of being accurately assayed in the pure state. (School of Pharmacy, University College, Nottingham.)

An Improved Method for the Assay of Strong Ointment of Mercuric Nitrate. Wm. R. Heading.* The proposed method consists of heating the ointment with 50 per cent. aqueous potassium hydroxide for about thirty-five minutes in the presence of zinc dust. The mercury is set free first as mercuric oxide, which is now reduced to metal by the hydrogen generated from the action of the alkali on the zinc. An amalgam is formed with the excess of zinc and the mercury is thus obtained quantitatively in a granular form, which may be easily freed from soap by decantation, filtration and washing. The amalgam is next dissolved in nitric acid, and the mercury determined by means of ammonium thiocyanate, the presence of zinc as nitrate being quite without effect. Compared with the official assay of this ointment, the new method, without loss of accuracy, affords considerable advantages in convenience and speed. (School of Pharmacy, University College, Nottingham.)

The Stability of Mixtures of Hydrogen Peroxide and Ethyl Alcohol. W. A. Woodward and J. Pickles.* It is shown that mixtures of ethyl alcohol and hydrogen peroxide (10 vols.) when dispensed and stored under certain conditions give rise to yields of acetaldehyde and acetic acid possessing clinical significance in the treatment of otitis media. The residual peroxide content of mixtures is shown to be less than that of corresponding solutions of peroxide stored separately. In order to avoid the formation of undesirable oxidation products and also to maintain maximum anti-

septic value, mixtures of this type when ordered for long periods should always be dispensed separately. Amber-tinted glass bottles should be used for dispensing the peroxide drops. Failing this, the patient should be instructed to keep the bottle in a cool and dark place. (Pharmaceutical Department of St. Thomas's Hospital, London.)

The Composition and Stability of Donovan's Solution. C. Morton and F. R. C. Bateson.* Determinations of the elevation of the freezing point, produced by adding successive increments of mercuric iodide to aqueous solutions of arsenious iodide, lead to the conclusion that such solutions contain in general more than one complex electrolyte. The solute in the Pharmacopœial solution has the approximate composition $\text{HgI}_2 \cdot 2\frac{1}{2}\text{HI}$, and consists of a mixture of the compound $\text{HgI}_2 \cdot 2\text{HI}$ with a second complex electrolyte containing a higher proportion of hydrogen iodide. Similar conclusions are arrived at from the results of conductimetric and potentiometric titrations. Under normal conditions of storage, oxidation of the tervalent arsenic in Donovan's Solution takes place to the extent of only about 7 per cent. in three months, and is incomplete after three years. (University of London).

The Assay of Phenazone (Antipyrin). H. Brindle.* Bougoult's method for the assay of antipyrin and Kolthoff's modification are shown to give results which, according to the purity of the reagents used, are from 0.3 to 1.0 per cent. too high, unless blank determinations are carried out. Fairly accurate results are obtainable by introducing a correction for the amount of iodine used up by the reagents, but the following process offers advantages over both methods in convenience and accuracy: 0.2 gram of antipyrin and 2 grams of sodium acetate are dissolved in 20 cc. of water in a stoppered flask and 30 cc. of N/10 iodine solution added. The flask and contents are allowed to stand with occasional shaking for twenty minutes. The precipitate is then dissolved by adding 10 cc. of chloroform and shaking and the excess of iodine titrated with N/10 sodium thiosulphate solution. The amount of iodine reacting with the reagents is determined by repeating the process, omitting the antipyrin or pref-

erably using only 10 cc. of N/10 iodine for the blank determination. An allowance is made for the iodine which reacts with reagents. (Pharmaceutical Department, Manchester University.)

A Note on Mercuric Oxycyanide B. P. F. C. J. Bird.* The B. P. requirement that this salt should be soluble in 18 parts of water should be altered to: One part should readily dissolve in 18 parts of boiling water with only a trace of residue, and the liquid should remain clear when cooled to 15.5 degrees C. As regards its behaviour toward heat, at quite a moderate temperature the dry salt darkens in color and decomposes very readily, and even when moist it is liable to deteriorate in color if exposed to a very gentle heat. On the other hand, a strong solution can undergo prolonged and vigorous boiling without change. The U. S. Dispensatory (1926 Ed.) gives the solubility of $\text{HgO} \cdot \text{Hg}(\text{CN})_2$ (the so-called normal oxycyanide) as 1 in 17, a figure obviously inaccurate. A solution of 1 in 200 attacks ordinary steel instruments very energetically. As little as 1 per cent. of the weight of the oxycyanide used of sodium carbonate will prevent this. Stainless steel is quite unaffected under similar conditions. In preparing solutions of mercuric oxycyanide, the salt should be dissolved in about 40 parts of boiling water, and then sufficient cold water added to produce the required degree of dilution. (Laboratories of National Drug Industries, Ltd.)

The Determination of Sulphur and Phosphorous in Medicaments after Oxidation with Perchloric Acid. Ernest Kahane. *Journ. Pharm. et Chim.* 19, 26-36 (1934). The author has developed a modified Kjehldahl flask, the use of which minimizes loss of sulphur during oxidation. The modification consists in attaching a bubbler type condenser bent in the form of the letter W to the outlet of the Kjehldahl flask, connection being made by a ground-glass joint. To determine sulphur, 0.1 to 0.2 gram of the substance to be tested is weighed accurately, placed in the flask, and 0.5 cc. of 10 per cent. iodic acid anhydride and 2 cc. of a mixture of 2 parts of perchloric acid (1.61) and 1 part of nitric acid (1.39) are added. A glass

*Summaries of papers contributed to the Science Sessions of the British Pharmaceutical Conference, 71st Annual Meeting, July 16-20, Leeds. From the *British and Colonial Pharmacist*, 87, 212-218 (1934).

bead is placed in the flask. Into the open end of the condenser is placed 0.5 cc. of iodic acid and sufficient water to effect a seal in the bent portion of the tube.

The reaction sometimes starts spontaneously, but generally it is necessary to heat the mixture. After the completion of the reaction, which is evidenced by quiet ebullition and decolorization of the solution, the apparatus is permitted to cool after which the liquid in the condenser is added to that in the flask by turning the former through an angle of 180 degrees. After boiling, the mixture is cooled, transferred to a 200 cc. graduated flask, and the excess of iodic acid reduced with a 10 per cent. solution of hydrazine hydrate. When the solution is decolorized it is neutralized with N/10 sodium hydroxide in the presence of phenolphthalein and the sulphur is determined by precipitation with barium chloride. Excellent results were obtained in the analysis of sulphur, sodium hyposulphite, ammonium thiocyanate, camphor-sulphonic acid, saccharin, thiosinamine, cystine and sulphonol.

For the determination of phosphorus, 2 or 3 cc. of a mixture of 1 part of nitric acid (1.39) and 2 parts of perchloric acid (1.61) are used in the case of products which are decomposable with nitric acid, or with a mixture of 10 cc. of nitric acid and 4 cc. of sulphuric acid (1.80) followed by nitric and perchloric acids where required. The phosphorus is then determined by precipitation as magnesium ammonium phosphate, ammonium phosphomolybdate or as the phosphomolybdo-ether complex according to the procedure of Copaux.

Detection of Gelatin in Milk Products. K. Braunsdorf. *Z. Unters. Lebensm.* 67, 326-332 (1934). Through *British Chemical Abstracts, Chem. & Industry*, 53, 522 (1934). The method depends on gelatin reacting as a protective colloid to cadmium sulphide. The material is heated to boiling, acidified with acetic acid, and filtered. Cadmium chloride is added, and hydrogen sulphide passed in. In the absence of gelatin, cadmium sulphide is precipitated, in the presence of gelatin a colloidal solution is formed. As little as 0.025 per cent. of gelatin can be detected. Agar and tragacanth have no effect. Milk products, which appear to have 0.1 per cent. of gelatin when tested by the picric acid method, react negatively to this test.

MEDICAL AND PHARMACEUTICAL NOTES

DI-NITRO-PHENOL AND PREPARATIONS MUST BE LABELED POISON—The use of Di-Nitro-Phenol and preparations of this dangerous chemical for the purpose of reducing excessive body weight is receiving considerable attention in the medical and lay press. Competent observers among the medical profession have cautioned those who are administering or using this chemical to take heed of its toxic properties. This drug and preparations thereof should be used only under competent medical supervision. It should not be sold promiscuously, nor should its use be advised by pharmacists. Customers purchasing the drug or proprietary preparations of it should be cautioned against its indiscriminate use.

In order to safeguard the public and to warn prospective users of its toxic properties, it will be required in the State of New Jersey that all preparations of Di-Nitro-Phenol, as well as the chemical itself, must be labeled "poison" under the provisions of Schedule A of Section 6 of the Pharmacy Act, and that sales of this chemical and preparations containing it must be registered. The requirements for selling poisons listed in Schedule A are as follows: "It shall be unlawful for any person in this State to sell or deliver to any minor under twelve years of age or to any persons known to be of unsound mind or under the influence of liquor, any of the substances enumerated in Schedule A or Schedule B appended to this section or any other poisonous drug, chemical or medicinal substance.

"It shall not be lawful for any person to sell at retail, give away or dispense any of the poisons enumerated in 'Schedule A' appended to this section or any other substance commonly recognized as a deadly poison, or any substance which according to standard works on medicine, materia medica, or toxicology, is liable to be destructive of adult human life in doses of five grains or less, without distinctly labeling with a red label the package, box, can or container or wrapper in which said poison is contained, with the name of the article in English and the word 'poison' and the name and place of business of the dispenser, and before delivery shall be made, the seller must first learn by inquiry that the person to whom delivery is made is aware of the dangerous character of the poison and is a proper

person to purchase such poison, and that it is desired for a legitimate purpose, and, before making such delivery, the seller shall record in a book kept solely for that purpose the date and hour, the name of the article, the quantity delivered, the use stated by the purchaser, and the name and address of the purchaser, which poison record shall be preserved for at least five years after the date of the last entry, and shall at all times be open to the inspection of any member or agent of the Board of Pharmacy of the State of New Jersey, or to any proper officer of the law."—*Board of Pharmacy, New Jersey.*

THE BIOLOGICAL EFFECTS OF THYMUS EXTRACT. L. G. Rowntree, J. H. Clark (by invitation) and A. M. Hanson (by invitation). Philadelphia Institute for Medical Research, the Laboratories of the Philadelphia General Hospital, Philadelphia, Pennsylvania, and the Hanson Research Laboratory, Faribault, Minnesota.

White rats (Wistar strain) have been injected intraperitoneally daily for nine months with an extract of thymus prepared by Hanson. In the first generation (F_0) treated test animals were heavier, bred more frequently, had larger litters of heavier average weight per rat; the control animals cast five litters, totalling twenty-two rats, the thymus treated pair nine litters, totalling eighty-six rats. Little of note appeared in the second generation (F_1) except somewhat more rapid development, somewhat earlier eruption of teeth and earlier descent of testes, twenty-two to twenty-nine days. This tendency becomes more pronounced with succeeding litters. In a seventh litter (L. F.) the animals were larger, body hair was visible almost from the beginning, and teeth erupted on the second day.

The third generation of thymus treated animals (F_2), as judged from forty-three surviving rats, evidenced rapidity of development almost beyond belief. Average birth weight was 5.3 grams; controls 4.4 grams (18 animals). Teeth appeared and ears opened on the first and second day. Animals were completely covered with hair and eyes opened on the fourth to sixth day. Testes descended on the twelfth and vagina opened on the twenty-third to the thirty-first day. Estrus was established from the thirtieth to fortieth day. The female of one pair (L_2F_1), injected from birth, cast a litter at forty-two days. The growth curves of third generation thymus treated

rats compared with controls revealed marked acceleration with the maximum difference about the sixteenth day and approached each other after the sixtieth day. Treated animals appear unusually docile and contented.

The effects of treatment which is continued through the grandparents and parents (acceleration in the rate of development) are much more marked on the offspring (third generation) than those resulting from continuous treatment for the same length of time confined to parents alone (seventh litter first generation).

It is evident, therefore, that this thymus extract has accelerated growth, development, maturity and fertility. The effects of thymus extract become progressively more pronounced as treatment is continued into succeeding generations.—From *The American Journal of Physiology*, Vol. 109, No. 1, July, 1934.

Atabrine

Atabrine is an alkyl-amino-acridine derivative, related to methylene blue, and is a yellowish, bitter powder, soluble in water to the extent of 7 per cent.

It was synthesized in 1930 by Mietsch and Mauss in the Scientific Research Laboratories in Elberfeld, Germany. Kikuth, following the method of Roehl in the study of plasmochin, found that atabrine was a schizonticide in rice-bird malaria, but had no effect on the gametes which, however, were rapidly destroyed by plasmochin which, in turn, was ineffective in the eradication of the schizont forms. Mühlens states that he has found a combination of the two in the ratio of plasmochin 1 part to atabrine 10 parts useful in the treatment of malaria.

HOSPITAL FORMULAS

Note: Most of these formulas are recommended for inclusion in the forthcoming revision of the *British Pharmaceutical Codex* (1934).

Injectio Peptoni

Peptone	50 gm.	1 oz.
Sodium Chloride	9 gm.	78¾ gr.
Sodium Hydroxide	a sufficient quantity	
Phenol	5 gm.	43¾ gr.
Sterilized Water for Intra- venous Injections	to 1000 cc. to 20 fl. oz.	

Dissolve the peptone and the sodium chloride in about 900 cc. (18 fluid ounces) of the sterilized water with the aid of heat. Add to the solution a 1 per cent. w/v solution of sodium hydroxide in the sterilized water until the liquid is neutral to litmus or to phenol red; dissolve the phenol in the product, filter and pass sufficient of the sterilized water through the filter to produce the required volume; sterilize by heating in an autoclave, by tyndallization or by filtration.

Note: When *Injectio Peptoni* is required for intramuscular injection, it should be prepared with 75 grammes (1½ ounces) of peptone.

Injectio Quininae et Aethylis Carbamatis

Quinine Hydrochloride ...	13.33 gm.	232¾ gr.
Ethyl Carbamate	6.67 gm.	116¾ gr.
Sterilized Water for Intra- venous Injections	to 100.00 cc. to 4 fl. oz.	

Sterilize by heating in an autoclave, by tyndallization, or by filtration.

Injectio Sodii Morrhuae

Sodium Morrhuate	50 gm.	1 oz.
Alcohol (90 per cent.)	10 cc.	96 m.
Distilled Water	to 1000 cc. to 20 fl. oz.	

Sterilize by heating in an autoclave, by tyndallization, or by filtration.

Note: When solid matter separates, it should be redissolved by warming, and the injection should be used with a syringe, previously warmed.

Injectio Thiosinaminae et Sodii Salicylatis

Thiosinamine	10.0 gm.	175 gr.
Glycerin	5.0 cc.	96 m.
Sodium Salicylate	13.8 gm.	241½ gr.
Distilled Water	to 100.0 cc. to 4 fl. oz.	

Sterilize by tyndallization or by filtration. It should be recently prepared.

Mistura Quininae Salicylatis

Ammoniated Solution of

Quinine	62.5 cc.	1¼ fl. oz.
Potassium Citrate	22.9 gm.	200 gr.
Sodium Salicylate	22.9 gm.	200 gr.
Glycerin	125.0 cc.	2½ fl. oz.

Compound Infusion of

Gentian	to 1000.0 cc. to 20 fl. oz.	
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Pilulae Phenolphthaleini Compositae

(Synonym: Pilulae Phenaloini.)

Aloin	0.19 gm.	3 gr.
Phenolphthalein	0.39 gm.	6 gr.
Strychnine	0.01 gm.	3/20 gr.
Dry Extract of Belladonna ...	0.06 gm.	1 gr.
Powdered Ipecacuanha	0.05 gm.	4/5 gr.
Syrup of Liquid Glucose	a sufficient quantity	

Mix to form a mass, and divide into 12 pills.

Pulvis Barii Sulphatis Compositus

(Synonym: Barium Meal; Shadow Meal.)

Barium Sulphate	750 gm.	12 oz.
Cocoa, of commerce	94 gm.	1½ oz.
Arrowroot	94 gm.	1½ oz.
Compound Powder of		
Tragacanth	31 gm.	½ oz.
Sucrose, in fine powder	31 gm.	½ oz.

SOLID EXTRACTS

Charles Lamb, it was, who coined the famous couplet,

"For thy sake Tobacco, I—
Would do anything but die!"

Yet this habit-forming weed, with its content of toxic nicotine, gives the lie to Elia—for if we believe some of the latest researches on tobacco, no one ever really becomes immune to its siren venom. Wright and Moffatt, in the *Journal of the A. M. A.*, conclude a recent research thus:

"The smoking of tobacco in the form of 'standard' cigarettes produces in the great majority of normal individuals certain definite pharmacologic effects: A marked drop in surface temperature occurs at the tips of the fingers and toes. This varies in different individuals with the same tobacco and in the same individual at different times. The average drop in the series was 5.3 degrees F.; the maximum drop was 15.5 degrees F.

"Certain subjects showed marked toxic effects from smoking one cigaret under controlled conditions. In each instance, these were experienced smokers who ordinarily note slight or no symptoms from smoking."

The Philosopher of Nazareth exhorted his flock to consider the lily, how it toiled not, nor spun, yet lived its lily life in hallowed loveliness.

Consider the trout, exhorts a modern physiologic philosopher—and pacify your pancreas.

Easy living is hard on parts of the pancreas that produce insulin; abstemiousness tends to repair the damage.

This has been recently shown in the case of fish by Dr. Walter N. Hess of Hamilton College. Dr. Hess used rainbow trout as his subjects. Some of them he overfed, others he put on a diet too high in fat-forming foods, and still others he fed normally but kept under-exercised.

In all cases, the islets of Langerhans in the pancreas, which are the insulin-producing areas, diminished in number and degenerated in condition. However, Dr. Hess put similarly pampered trout on a diet

low in fat-producing materials, and after a while the damaged tissue showed considerable regeneration.

The Gallic trick of planting "a stick" of whiskey or cognac in his coffee—assuming that Gallic coffee is ever truly coffee—now finds support from science. For the coffee cramps the liquor's kick and keeps it tame and tasty. Several persons were given varying amounts of alcohol, according to the degree of their resistance to its effects. The doses ran from 30 to 75 cubic centimeters of grain alcohol, diluted with twice the quantity of water—roughly the equivalent of a drink or two of anyone's gin. Their degree of intoxication was measured in two days: by the amount of secretion from one of the salivary glands, and by the number of errors made in trying to follow a moving object with a slender beam of light.

It was found that about a pint of coffee, made by a uniform method and moderately strong, was required to counteract the effects of the alcohol, if taken at the same time with it. Coffee taken after the alcohol had less effect in cancelling out the latter drug.

Fog dispersion is a recent achievement of the physical chemist. The other day an experimenter on the staff of the M. I. T. demonstrated up in South Dartmouth, Mass., that droplets of "thirsty" water scattered in foggy air would virtually devour all the fog particles near them and then drop to the ground as air. The "thirsty" water was a solution of the hygroscopic calcium chloride.

A long-awaited fog was stripped of its invisibility in a section 30 feet high, 100 feet wide and about one-half mile long.

Metchnikoff, who died much too soon to prove his own case, stressed the longevity of the peoples of certain countries in which acid milk drinks formed an important part of the regular diet. He suggested the use of these lactic-acid-forming organisms as a means of holding in check the putrefactive processes of the intestinal tract and so living to an over-ripe old age! More recent evidence indicates that *Lactobacillus acidophilus*, a hardier competitor of the variegated flora of the intestinal canal, may predominate to the exclusion of undesirable bacteria. Acidophilus milk may, therefore, actually be of considerable aid to therapeutics, and is receiving the recommendation of physicians in certain cases of intestinal disturbance.

"Dreft" is a spray-dried soap substitute offered in flakes as a new detergent. Actually it is a sodium salt of sulphated alcohols obtained by fractionally distilling coconut and palm oils. It is soon to be offered as a bland soap bar for toilet use and as a shampoo. Originally conceived as a wetting-down agent for textiles, this and analogous products are finding new applications every day.

Authors may find it a hardship to "live on their books," yet bacteria can live on their pages for months.

The best books may be a great source of danger if a careless tubercular person used them last, for researchers have found that the germs live on the pages for four or five months. The question is regarded as of practical importance because it shows the necessity of disinfecting books circulating in public schools or libraries.

Tests have been made to see how long the germs from tubercular sputum and from a laboratory culture kept their virulence when smeared on the pages of a large number of books kept in all sorts of conditions such as are found in homes, schools, and libraries. The germs from sputum were the hardiest and were able to infect guinea pigs with the disease even after four and a half months. The germs from the laboratory cultures were still active after two months, but in about three months they were impotent.

Permutizing water is the special term for taking out of water the bases that make it "hard"—to lather with soap—and replacing them with sodium, a base that will "soften" the water. Thus a hard calcium water becomes a soft water. Zeolite is the "medium of exchange." Now comes a chemist who proposes, in effect, to do the same thing with milk, and so reduce its calcium content, and form a more digestible flaky curd when the milk finally finds the stomach.

Therapeutic color schemes may result in turning out patients from surgical clinics as gaudy as Easter eggs. For in addition to the already colorful antiseptics, mercurochrome, gentian, violet, the picrates, etc., word has come that malachite green and brilliant green, verdant as any vale in Erin, outsmart all other dyes in killing skin bacteria.